## REMARKS

Claims 1, 2, 4-8, and 21-24 are currently pending in the application. Claims 3, 9-20, and 25-42 have been canceled. Claims 1, 6, and 21 are in independent form.

Applicant's attorney wishes to thank the Examiner for the courtesies extended in a telephonic interview that was conducted November 9, 2004. During the interview the Examiner raised several potential enablement rejections with regard to the delivery of the mRNA. In order to further prosecution, the claims have been amended to recite that the mRNA is directly administered to the cells. Reconsideration of the rejection is respectfully requested.

Claim 3 is objected to under 37 CFR 1.75(c), as being in improper dependent form for failing to further limit the subject matter of a previous claim. In response thereto, Applicants have canceled claim 3 without prejudice in order to further prosecution. Reconsideration of the objection is respectfully requested.

Claims 7 and 8 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office Action states that it is unclear how protein synthesis can be increased from endogenous protein in the cells as protein synthesis is from mRNA. In order to further prosecution Applicants have amended claim 7 without prejudice to recite "from endogenous mRNA in the cells." Reconsideration of the rejection is respectfully requested.

Claims 1-5 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, in that the claims contain subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action holds that the claims encompass a genus of molecules wherein the genus comprises thousands, possibly millions, of different mRNAs considering that the genus encompasses all mRNAs encoding "proteins that are desired to be upregulated in a cell." The Office Action further holds that Applicants have not described any structural or functional elements of the mRNA sequences that are common to all of the members of the genus Further the Office Action holds that, there is no description describing where, in the structure, there is conferred the desired function.

It is respectfully submitted that one skilled in the art would know the mRNA related to protein synthesis that can be used in the method of the present invention. The mRNA in the present invention need not be limited to one particular structure or one particular mRNA, because any mRNA can be utilized in conjunction with the methods of the present invention. The structural element common to all members of the genus is that the members must all be mRNA related to protein synthesis. Such a description is sufficient for one of skill in the art. Examples of mRNAs that can be used in conjunction with the method of the present invention are set forth in the specification at pages 11, lines 8-25 and page 23, lines 16-18. Additionally, several claims have been amended to recite that the mRNA encodes either an elongation factor or a translational regulatory protein both of which are disclosed in the application as filed. The mRNA can be isolated from numerous sources including rat mRNA and human mRNA. Since the specification supports the claims as pending, reconsideration of the rejection is respectfully requested.

Claims 1-5 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention. More specifically, the Office Action holds that one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation. However, there would not be any undue experimentation because any sequence encoding mRNA that is related to protein synthesis can be used in the method of the present invention. Examples of such sequences are well known to those of skill in the art and are supported by the specification as filed, therefore no undue experimentation would be required to perform the claimed method. Accordingly, reconsideration of the rejection is respectfully requested.

Claims 6-8 and 21-24 stand rejected under 35 U.S.C. 112, first paragraph as based on a disclosure which is not enabling. Specifically, the Office Action holds that claims 6 and 21 are drawn to methods wherein method steps that are critical or essential to the practice of the invention are not included in the claims. Namely, the Office Action holds that claim 6 does not method steps for increasing the protein synthesis in the cells and claim 21 does not include method steps for increasing the protein synthesis in the wound. In order to further prosecution, Applicants have amended claims 6 and 21 to include thesuggested steps, specifically, of delivering mRNA to the cells and potentiating an increase of protein synthesis in endogenous mRNA in the cells. Reconsideration of the rejection is respectfully requested.

Claims 1-8 and 21-24 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for the full scope encompassed by the claims. The Office Action holds that the specification does not enable any person skilled in the art to make/use the invention commensurate in scope with the claims.

The Office Action holds that the claims encompass methods for increasing the expression of any mRNA in a cell for any reason, and therefore

encompass a very wide array of patently distinct methods. Further, the Office Action holds that there are no working examples of methods other than wound healing, and that additional experimentation would be required to practice the broadest claimed methods in their full scope. It is respectfully submitted that the specification as originally filed supports the claims as pending. Specifically, the claims recite a method for augmenting protein synthesis in a cell by administering mRNA functionally related to protein synthesis, thereby augmenting endogenous protein synthesis. As defined in the specification as filed, "augmenting" is intended to include both increasing cell growth and decreasing cell growth, as necessitated by the cells to which the method is applied. Support for this is disclosed on page 9, line 29 through page 10, line 5 wherein there is disclosed that that method increase protein production, the state of the cell at the time of treatment dictates whether such an increase will lead to cell proliferation or cell death. A cell is programmed for a particular genetic response by the signals that it receives *in vivo*. It is because of this first priming of the cell's response to its environmental signal that an increase in protein synthesis can enhance a cell to increase the synthesis of any "desired" protein. The "desired protein" is predetermined by the signal causing the genetic response to produce the mRNA. Augmenting protein synthesis will only turn up the response to whatever the cell has been primed to do based on an initiating signal such as wound healing, or cell growth or apoptosis. The response is an outcome of the state of the cell. Thus, an increase in protein synthesis will be determined for a particular cell by the state of that cell. The outcome of increased protein synthesis for cells in a particular environment cannot be random; it is determined by the endogenous cellular mRNA. The outcome of increased protein synthesis can in fact be predicted based on the cell and its environment, therefore one of skill in the art can predict the outcome of a treatment utilizing the methods of the presently pending claims.

The Office Action further holds that it is known in the prior art that administering mRNA encoding growth factor EGF can be administered to wound cells and result in the transient increase in synthesis of the growth factor in the cells which leads to faster wound healing (Sohn, et al.). Further, the Office Action holds that simply increasing the synthesis of translational regulatory proteins can turn normal cells into cancerous cells, thus making it unpredictable how a nucleic acid encoding a translational regulatory protein can be administered to a cell and result in the desired outcome without transforming the cells into cancerous cells. Administration of DNA encoding either EGF (Andree, et al.) or eIF4E (Lazaris-Karatzas, et al.) transformed normal cells into cancerous cells due to the lasting nature of the DNA administration. In contradistinction, the methods of the presently pending claims recite augmenting endogenous protein synthesis. In other words, the claimed method recites administering mRNA that in turn augments the endogenous mRNA protein synthesis, such that the result is dependent upon the state of the cell at the time of treatment. In essence, the method of the presently pending claims turns on an already existing switch that regulates protein synthesis. The prior art methods utilized DNA and as such the prior art studies were riddled with problems. The DNA transformed the cells, such that the synthesis of proteins was outside of normal parameters. Applicant's method of mRNA administration circumvents this concern. The administered mRNA is *predictably* transient since it is destroyed by the normal mechanism of cellular mRNA degradation. Moreover, the data of Table 4 in the specification demonstrates that the response to mRNA administration is transient, being completely lost within 48 hours, thereby eliminating the potential transformation of a normal cell to a cancerous cell.

Claims 1-6, 21 and 22 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Sohn, et al. (Wound Rep. Reg. 2001). Reconsideration of the rejection under 35 U.S.C. § 102(b), as anticipated by Sohn, et al. reference, as applied to the claims is respectfully requested. Anticipation has always been held

to require absolute identity in structure between the claimed structure and a structure disclosed in a single reference.

In Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986) it was stated: "For prior art to anticipate under §102 it has to meet every element of the claimed invention."

In Richardson v. Suzuki Motor Co., Ltd., 868 F.2d 1226, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989) it was stated: "Every element of the claimed invention must be literally present, arranged as in the claim."

The Office Action holds that the Sohn, et al. reference teaches a method of augmenting wound healing by delivering exogenous mRNA encoding the growth factor EGF to wound cells using particle acceleration to deliver the mRNA to the cells wherein the method results in an increase of protein synthesis of the mRNA delivered into the cell (which is then endogenous) such that the method results in a transient increase in protein synthesis in the cell, thereby augmenting healing of the wound. The Sohn, et al. reference teaches the biolistic delivery of mRNA encoding EGF to wound cells. The mRNA that was delivered is translated inside the cell, and the administered mRNA is responsible for wound healing. It is the EGF encoded in the exogenous mRNA that promotes wound healing. In contradistinction, the presently pending independent claim recite a method of delivering mRNA functionally related to protein synthesis to cells, whereby the delivered mRNA causes endogenous mRNA in the cell to synthesize protein. The delivered mRNA is not solely responsible for wound healing. Instead, the delivered mRNA induces endogenous mRNA encoding elongation factors to be translated. (See Table 4 of the specification as filed.) It is the endogenous mRNA that augments protein synthesis in the cells after being initiated to do so by the delivered mRNA.Since the Sohn, et al. reference does not disclose the potentiation of endogenous mRNA from the delivery of mRNA functionally related to protein

synthesis of the presently pending independent claims, the claims are patentable over the Sohn, et al. reference and reconsideration of the rejection is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above. The prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

KOHN & ASSOCIATES, PLLC

Kenneth I. Kohn, Reg. No. 30,955
30500 Northwestern Highway, Suite 410
Farmington Hills, Michigan 48334
(248) 539-5050

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I hereby certify that this correspondence is being transmitted via facsimile (703) 872-9306 to the Patent and Trademark Office on November 30, 2004.

Connie Herty